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# The use of optical coherence tomography (OCT) to evaluate the efficacy of different photocoagulations in diabetic macular edema treatment

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**Abstract. – OBJECTIVE: To evaluate the therapeutic effects of the early application of photocoagulation for treating the macular edema in non-proliferative diabetic retinopathy (NPDR). We also wanted to evaluate the potential of optical coherence tomography (OCT) to make a quantitative detection in patients suffering from this condition.**

**PATIENTS AND METHODS: From October 2010 to October 2014, a total of 132 patients, all diagnosed with NPDR combined with clinically significant macular edema (CSME) in our hospital, were enrolled in this study. After obtaining the approval of the hospital Ethics Committee and the informed consents of patients and families, we divided the cases into two groups: PRP group (n=63) and macular edema group (n=69). Clinical effects and complications associated with the used methods were compared and analyzed in two groups.**

**RESULTS: We analyzed the panretinal photocoagulation (PRP), and macular grid photocoagulation curative effects. The difference in successful surgery rate, between the two groups, was not statistically significant ($p > 0.05$). When we examined patients 1 month, 3 months, and 6 months after the surgery, average retinal thickness and volume in macular region in both groups were reduced. In the group, the comparison was statistically significant ($p < 0.05$) while between the groups, the comparison was not statistically significant ($p > 0.05$). Visions in both groups were improved after treatment and difference on the post-operative 6-month vision improvement degree between the two groups was not statistically significant ($p > 0.05$).**

**CONCLUSIONS: We concluded that the early photocoagulation could significantly improve the vision. However, the clinical effects and complications associated with the use of PRP and macular grid photocoagulation had no significant differences.**

*Key Words:*
NPDR, CSME, PRP, Macular grid photocoagulation.

## Introduction

Diabetic retinopathy (DR) is a serious eye complication and a major cause of blindness related to diabetes mellitus. The three major factors leading the DR to blindness are as follows: (i) Macular edema, (ii) traction retinal detachment incurred from vascular proliferation, and (iii) vitreous hemorrhage. Among these factors, diabetic macular edema (DME) has the most devastating effects. Incomplete epidemiological investigation[1] revealed that the incidence of macular edema in nonproliferative diabetic retinopathy (NPDR) was about 10.5 to 36.7%. Currently, there is no ideal therapy for patients suffering from macular edema. Although photocoagulation was developed very rapidly, clinical follow-ups found that as much as 60% of proliferative DR patients were suffering from vision loss in spite of multiple or repeated photocoagulation treatments. Besides, their complications were quite serious. There are few reports on photocoagulation treatment for NPDR and clinical significance of diabetic macular edema (CSME) in the literature. The same can be said for prospective studies on two different photocoagulation methods. In order to shed more light on the issue, we adopted the optical coherence tomography (OCT) to make quantitative analyses on our patients.

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## Patients and Methods

### Patients

From October 2010 to October 2014, a total of 132 patients all diagnosed with NPDR combined with clinically significant macular edema (CSME) in our hospital were enrolled in this work. NPDR diagnostic criteria employed in this study was the criteria found in the International clinical diabetic retinopathy severity classification[2] and for CSME diagnostic criteria we used the 2003 Sydney International clinical classification[2]. *Mild edema*: some retinas were thickened or had hard exudates, which were far from the macular center; *moderate edema*: retinas were thickened or had hard exudates, which didn't involve the macular center; *severe edema*: retinas were thickened or had hard exudates, which involved the macular center. Inclusion criteria: (1) moderate and severe NPDR with moderate and severe macular edema, (2) vision ≥0.1, refraction≤±3.00DS, central fixation, (3) first photocoagulation treatment and blood sugar control reached to the standard, without other ocular diseases, such as severe glaucoma, cataract, infection, etc. Exclusion criteria: (1) patients with severe heart, liver, kidney and other organ dysfunctions; (2) patients with laser allergy, incomplete clinical materials, poor compliance, and that refused the study, etc.

After obtaining the approval of the hospital Ethics Committee and the informed consents of patients and families, we divided the cases into two groups: PRP group (n=63) and macular edema group (n=69). PRP group consisted of 42 males and 21 females, aging from 48 to 72 years, with an average age of (57.4±12.3) years; 29 cases were diagnosed with moderate NPDR and 34 cases with severe NPDR; 35 cases with moderate macular edema and 28 cases with severe macular edema. Grid macular photocoagulation group consisted of 45 males and 24 females, aging from 46 to 78 years with an average age of (58.5±14.2) years; 33 cases were diagnosed with moderate NPDR and 36 cases with severe NPDR; 37 cases with moderate macular edema and 32 cases with severe macular edema. The differences about gender, age, NPDR stage and macular edema grading between the two groups were not statistically significant ($p$ >0.05).

### Experimental Method

Laser treatments were performed by an experienced physician using VISULAS 532s solid frequency doubled laser from ZEISS Company, Oberkochen, Germany. One hour before laser treatment, 0.5% tropicamide was applied to make complete mydriasis, 0.4% oxybuprocaine was used twice for anesthesia, and 1% methyl cellulose was used to fill the laser mirror.

PRP: multiple wavelength krypton laser was applied, with a spot size of 300 μm (200 μm within the equator), and exposure time was 0.2s. Also with Tso grading of level III mild-moderate spot reaction (spots were rich white, with two light grey rings around. The white center was inner nuclear layer necrosis and the two light gray rings were outer nuclear layer necrosis and purpurogenous membrane necrosis, respectively). The range from 1 DD (disc diameter) outside optic disc to eye ground outside equator, and the posterior pole between macula and upper and lower vascular arches on the temporal side were avoided photocoagulation. Photocoagulation was completed in 3 to 4 times, each with 300-500 spots according

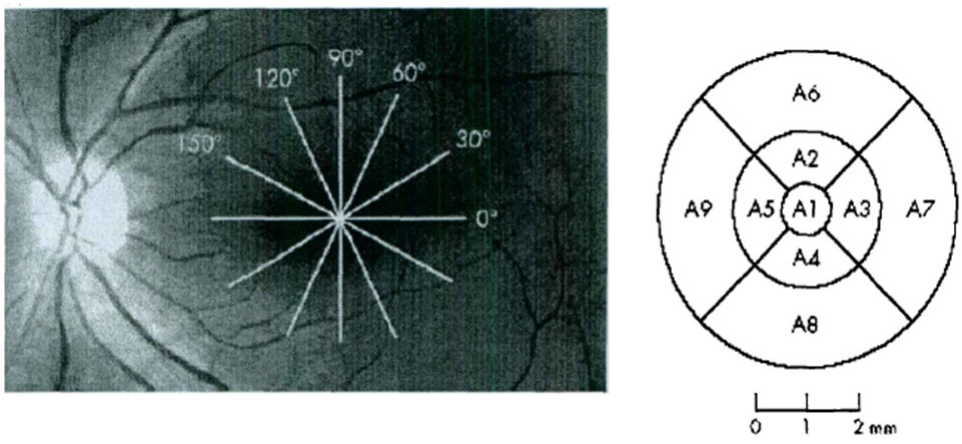


**Figure 1.** OCT zone illustration.

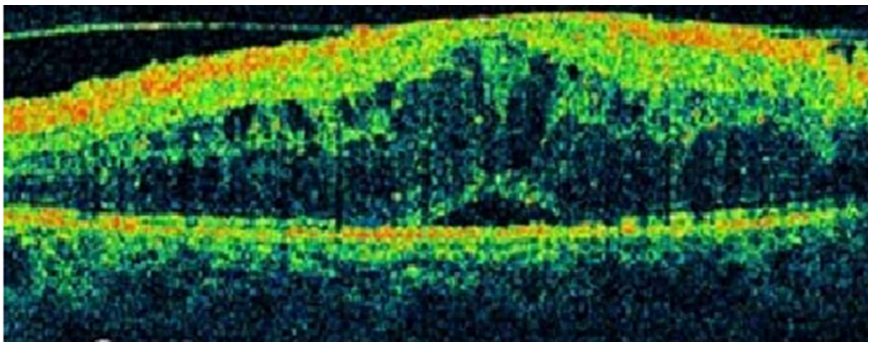

**Figure 2.** Under OCT, retinal layer showed diffuse sponge-like expansion, and retinas in and around macular area were thickened.

to the sequence from the inferior part, the nasal side, the upper part to the temporal. Photocoagulation was performed every 7 days. C shape grid photocoagulation was used in the macular area with a spot size of 100 μm, exposure time of 0.1s, Tso grading of level I, and the area within 500 μm from central fovea or disc and the optic disc macular bundle avoided photocoagulation.

### Observation Index

The operation success rate was evaluated. The average thickness and volume of the retina in macular region in 1 month, 3 months, and 6 months after the treatment were measured. The degree of vision improvement and the prevalence of complication in 1 month after treatment were recorded and differences between the two groups were studied. The thickness and the volume of the retina were measured using an OCT instrument from Zeiss-Humphrey (Carl Zeiss Shanghai Co. Ltd., Shanghai, China). Specifics were as follows: depth of scanning was 2 mm, length of scanning line was 4 mm, pixel was 500x500 and resolution was 10 μm. Before the examination, 0.5% compound tropicamide was used to make complete mydriasis. Patients were maintained in sitting position with lower jaw kept in collar supporter. During the examination, the affected eye was required to gaze at a solid viewpoint in the lens, radial linear scanning was selected and the intersection angle between each line was kept at 30°. Six clear images were recorded and stored on a computer. The macular section had 9 areas: the central area that was centered on the central viewpoint, with a diameter of 1 mm, the inner ring area with a diameter of 2.22 mm, and the outer ring area with a diameter of 3.45 mm. The inner and outer areas were divided by two radioactive rays into four parts: upper part, lower part, nasal part and temporal part. Computer image analysis software Retinal Topographic Map (RTM) was used to measure the thickness of retinal nerve epithelium in different areas. Morphological analyses were conducted to study the scanning images. Figure 1 illustrates the OCT and Figure 2 shows the macular edema.

### Statistical Analysis

Statistical software package SPSS 20.0 (SPSS Inc., Chicago, IL, USA) was used for data processing. Measurement data were presented by means±standard deviation ($\bar{x} \pm S$); *t*-test was applied

**Table I.** Average thickness and retina's volume in macular region (comparative data).

| Group | Before treatment | | 1 month | | 3 months | | 6 months | |
|---|---|---|---|---|---|---|---|---|
| | Retinal thickness (μm) | Volume ($mm^3$) | Retinal thickness (μm) | Volume ($mm^3$) | Retinal thickness (μm) | Volume ($mm^3$) | Retinal thickness (μm) | Volume ($mm^3$) |
| PRP group | 246.7±32.6 | 7.8±1.2 | 221.9±36.5 | 7.1±1.3 | 176.5±29.7 | 5.6±0.9 | 144.9±27.7 | 5.3±1.1 |
| Grid macular photo-coagulation group | 252.3±29.8 | 8.3±1.5 | 235.5±29.3 | 7.3±1.4 | 182.3±31.2 | 5.9±0.8 | 156.2±29.6 | 5.2±1.2 |
| *t* | 0.203 | 0.415 | 0.757 | 0.623 | 0.923 | 0.769 | 1.204 | 1.324 |
| *p* | 0.628 | 0.719 | 0.623 | 0.847 | 0.619 | 0.824 | 0.213 | 0.509 |

**Table II.** Vision improvement and complication occurrence in two groups.

| Group | Case | Pre-operative vision | 6 months after treatment | Aggravated edema vision | Worsened | Others | Complication incidence |
|---|---|---|---|---|---|---|---|
| PRP group | 63 | 0.2±0.1 | 0.6±0.2 | 5 | 3 | 2 | 10 (15.8) |
| Grid macular photocoagulation group | 69 | 0.2±0.1 | 0.6±0.2 | 6 | 2 | 3 | 11 (15.9) |
| $t(X^2)$ | | 0.958 | 0.765 | | | | <0.001 |
| $p$ | | 0.425 | 0.632 | | | | 0.991 |

for comparisons between groups; repeated measurement data analysis was applied for comparisons in the group; enumeration data were presented by percentage (%); the $X^2$ test was applied in comparisons between groups; $p$ <0.05 was considered to be statistically significant.

## Results

### Analysis of Post-operative OCT Measurement Data

In PRP group, 59 cases (93.65%) successfully completed their surgeries, 2 cases had an aggravated edema, 1 case had an infection and 1 case had a worsened vision. In grid macular photocoagulation group, 65 cases (94.20%) successfully completed their surgeries, 3 cases had aggravated edema and 1 case had worsened vision. The difference in successful surgery rate was not statistically significant ($p$ >0.05) when compared between the two groups. The average retinal thickness and volume in macular region in one month, three months, and six months after the surgery were reduced in both groups. While the comparison in the group was statistically significant ($p$ <0.05) the comparison between the groups did not reveal any statistically significant difference ($p$ >0.05) (Table I).

### Comparisons on Vision Improvement and Complication Prevalence

While both groups had improved visions after the treatment, the difference in vision improvement, 6-month post-operative, was not statistically significant ($p$ >0.05) between the two groups. The difference on the post-operative 1-month complication between the two groups was not statistically significant ($p$ >0.05) (Table II).

## Discussion

Prior studies[3] confirmed that the vision impairment of DR patients was not completely related to the DR staging, but closely linked to the lesion degree of the macular area. The pathogenesis of macular edema is considered the result of local retinal vascular endothelial cell barrier (inner blood retinal barrier) and retinal pigment epithelial cell barrier (outer blood retinal barrier) functional injuries. Usually, it involves multiple cytokines, such as VEGF, interleukin-2, interleukin-6 and other cytokines[4].

Early clinical manifestations of macular edema are not evident and this problem reduces the patient's chance to have a clear diagnosis. By the time the symptoms become evident, the vision has already been seriously affected, and patient already missed the optimal treatment opportunity, nevertheless OCT can help the situation and can increase the patient's chance to have a clear diagnosis[6]. With its 830 μm infrared ray, OCT can create tomography imaging on the eye tissue. OCT is characterized with optimal axial resolution, which could detect the subtle macular retinal thickening incurred from early macular edema. Besides, several studies have shown that OCT had a favorable repeatability in measuring retinal thickness. Therefore, compared to the conventional fundus examination and fundus fluorescein angiography (FFA), OCT is more sensitive and more direct for DME examination. Moreover, it can support repeated qualitative and quantitative analyses on the extent and the range of macular edema as well as the changes occurred in various tissues. OCT is also a better way to diagnose DME and tracing the curative effects of laser photocoagulation.

Several multi-center clinical trials[7,8] confirmed that photocoagulation was an effective treatment for vision loss incurred from DME. The

decision on whether to use photocoagulation and when to employ photocoagulation is widely based on the extent of the involvement of hard exudates after edema in macular center. Presently, photocoagulations mainly include local direct photocoagulation, PRP, grid macular photocoagulation, and improved grid macular photocoagulation. PRP is mainly applied in significant micro hemangioma and leakage cases[9]. Photocoagulation should be performed on focal leakage 500 μm within macular center, and microaneurysm with diameter less than 125 μm. Nerve fiber layer retinal hemorrhages (flame or debris hemorrhage) and spotted hemorrhages with diameter more than 125 μm should be avoided. The best treatment response of photocoagulation is when the microangioma becomes pale or darkened, without too large photocoagulation spot. Treatment mechanism is as follows: 1. Due to ischemia, inner retinas produce a kind of neovascular growth factor that could diffuse into other regions of retina through vitreum and stimulate the growth of neovascularization; 2. By breaking some high metabolic photoreceptor cells, which are conductive for oxygen to diffuse into inner layer of retina through choroidal capillary and improve the oxygen supply of the ischemic retina. Grid macular photocoagulation is principally favorable for diffuse macular edema and retinal non-perfusion area[10]. It could also be applied in retinal avascular area and small capillary hemangioma. But generally, it would not be used in the area that has already been photocoagulated.

Photocoagulation energy, sequence, time interval and the method can significantly influence the recovery degree and the recovery time in macular edema cases[11]. Therefore, quantitative detection of changes in retina's thickness and volume in macular region after photocoagulation is not only important for preventing and reducing the incidence of macular edema but also quite vital for improving the curative effects and vision prognosis of the patients. Our results showed that the differences observed in surgery success rates for both groups were not statistically significant. Average retinal thickness and macular region volume decreased in both groups in 1 month, 3 months, and 6 months after surgery. Comparison in group was statistically significant while comparison between groups was not. While patients' vision quality in both groups were improved, the differences between two groups were not statistically significant six months after the operation. Differences in one-month post-operative complications in two groups were not statistically significant.

## Conclusions

Early photocoagulation significantly improved vision, and PRP and macular grid photocoagulation had no statistical significance in clinical effects and complications. In clinic, different photocoagulations could be used for patient treatment with different OCT characteristics.

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### Conflict of Interests:

The Authors declare that they have no conflict of interests.

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